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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,075	12/30/2003	Clark A. Briggs	6017.US.D2	7952

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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 05/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/749,075	BRIGGS ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *1-22 and 39-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-35* is/are rejected.

7)☒ Claim(s) *36-38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 December 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/30/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 1 to 51 are pending in the instant application.

2) Claims 1 to 22 and 39 to 51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 15 February of 2006.

3) Claims 36 to 38 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must depend from other claims in the alternative only. Claim 36 is improper because it depends from claim 1 **and** claim 31. Claims 37 and 38 are improper because they depend from claim 36. See MPEP § 608.01(n). Accordingly, these claims not been further treated on the merits.

4) The drawings in the instant application do not comply with 37 C.F.R. § 1.821(d), which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. M.P.E.P. 2422.02 expressly states that "when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings". In the instant application, the text "(SEQ ID NO:_)" in lines 13 and 17 on page 4 should be completed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5) Claims 23 to 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5.1) Claims 23 to 35 are vague and indefinite because the metes and bounds of the limitation "a variant human α7 nicotinic acetylcholine receptor (nAChR) polypeptide" are undeterminable. The text on page 8 of the instant specification defines this term as encompassing "a polypeptide sequence that differs from the wild-type polypeptide in the substitution, insertion or deletion of one or more amino acids" and which "differs in primary structure (amino acid sequence), but may or may not differ significantly in secondary or tertiary structure or in function relative to the wild-type". Given the ambiguous definition provided by the specification, one of ordinary skill could not determine if a referenced polypeptide was encompassed or excluded by this limitation.

5.2) Claims 23 to 35 are vague and indefinite because there is no antecedent basis for "the wild-type human α7 subunit polypeptide". It has been well established in the art that there are minor variations in the amino acid sequences of almost all proteins within a given population of organisms. All of the natural variations in the amino acid sequence of a common protein within a species of organisms are "wild-type". Further, the number 274 requires a point of reference. Figure 3 on page 548 of the Peng et al. publication (Mol. Pharm. 45(3):546-554, 1994, of record) depicts the amino acid sequences of three proteins that are each identified therein as an α subunt of an acetylcholine receptor. The amino acid residue identified as threonine 274 in SEQ ID

NO:2 the instant application corresponds to the valine at position 254 in each of the sequences presented in the Peng et al. publication and to the valine at position 251 as depicted in Figure 1 on page 501 of the Galzi et al. publication (Nature 359:500-505, 08 Oct. 1992, of record). Therefore, these claims should probably refer to "a human α7 nicotinic acetylcholine receptor polypeptide having an amino acid substitution at a position corresponding to position 274 of SEQ ID NO:2".

5.3) Claim 24 is vague and indefinite because there is no antecedent basis for "the host cell".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6) Claims 23 to 25, 27, 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by the Galzi et al. publication (Nature 359:500-505, 08 Oct. 1992, of record). Because the broad definition of the limitation "variant human α7 nicotinic acetylcholine receptor (nAChR) polypeptide" provided by the specification encompasses unlimited amino acid insertions, deletions and substitutions relative to the amino acid sequence of a "wild-type" human α7 nicotinic acetylcholine receptor polypeptide, these claims encompass the assay that was described in Figure 4 on page 503 of Galzi et al., which employed a modified subunit of a chicken α7 nicotinic acetylcholine receptor polypeptide wherein a valine at a position corresponding to position 274 of a human α7

nicotinic acetylcholine receptor polypeptide depicted in SEQ ID NO:2 of the instant application has been replaced by a threonine.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7) Claims 23, 24, 27, 29 to 32, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Galzi et al. publication (Nature 359:500-505, 08 Oct. 1992, of record) in view of the Peng et al. publication (Mol. Pharm. 45(3):546-554, 1994, of record). The assay that was described in Figure 4 on page 503 of Galzi et al. can be distinguished from the claimed invention in so far as the instant claims relate to an assay that employs a mutant of a human α7 nicotinic acetylcholine receptor polypeptide comprising the amino acid sequence presented as residues 23 to 486 in SEQ ID NO:2 of the instant application. Whereas the α7 nicotinic acetylcholine receptor polypeptide employed by Galzi et al. contained a valine to threonine substitution at the position corresponding to 274 in SEQ ID NO:2 of the instant application and described by Galzi et al. as "the α7-4 mutant receptor" (V251T), that polypeptide was of chicken origin rather that human origin. The text bridging pages 502 and 503 of Galzi et al. disclosed that the single V251T mutation described therein increases receptor sensitivity and reduces desensitization, as described in the discussion of this reference contained in the second paragraph on page 2 of the instant specification.

The assay that was described in Figure 4 of page 549 of Peng et al. differs from the claimed invention only in so far as the human α7 nicotinic acetylcholine receptor polypeptide employed therein did not contain a valine to threonine substitution at the position corresponding to 274 in SEQ ID NO:2 of the instant application. Because one of ordinary skill in the art of receptor biology was well aware, at the time of the instant invention, that the information obtained from an assay like that of Galzi et al. was of greater value when it could be applied to human subjects, that artisan would have found

it *prima facie* obvious to have applied the structure/function analysis described therein to the human α7 nicotinic acetylcholine receptor polypeptide described in Figure 3 of Peng et al. One would have expected such a substitution to yield specific information regarding the human protein because the abstract of Peng et al. disclosed that the human and chicken α7 nicotinic acetylcholine receptor polypeptides demonstrated "a large species-specific pharmacological difference, despite small differences in α7 sequences".

In so far as the claims require monitoring for cytotoxicity, the abstract and Figure 4 of Peng et al. shown that the α7 nicotinic acetylcholine receptors described therein were known to bind α-bungarotoxin and, therefore, an artisan would have found it *prima facie* obvious to have employed the protein described therein to identify compounds that antagonize the action of toxins on that receptor. That artisan would have been motivated to employ a human α7 nicotinic acetylcholine receptor comprising a valine to threonine substitution like that described as V251T in Galzi et al. because such a mutant would have been reasonably expected to have increased sensitivity and a decreased rate of desensitization relative to the unmodified receptor since the amino acid sequences from this region of the human and chicken α7 nicotinic acetylcholine receptor subunits were known to be identical.

8) Claims 23 to 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Galzi et al. and Peng et al. publications as applied to claims 23, 24, 27, 29 to 32, 34 and 35 above, and further in view of the Elliot et al. patent (5,910,582). In so far as these claims encompass an assay that employs cells other

than the oocytes employed by Galzi et al. and Peng et al, the text beginning on line 46 in column 10 and going through line 18 in column 16 described the incorporation of recombinant polynucleotides encoding mammalian neuronal nicotinic acetylcholine receptors, and expressly including the human α7 nicotinic acetylcholine receptor of Peng et al., into mammalian host cells for the purpose of identifying agonists and antagonists thereto. To have employed a human α7 nicotinic acetylcholine receptor comprising a valine to threonine substitution like that described as V251T in Galzi et al. in such a host cell and assay because such a mutant would have been reasonably expected to have increased sensitivity and a decreased rate of desensitization relative to the unmodified receptor would have been prima facie obvious to one of ordinary skill in the art of receptor biology in view of this combination of references.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN ULM
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